PMUSA Clinical Evaluation Study* Plan Worksheet (DRAFT v. 8)

** Applies to Product Development Studies and Research Projects; for simplicity, will refer only to "Study" in this Plan.*

PMUSA CE Study Tracking Number: _____ *(MUST be used on ALL study communications)*

Clinical Program Leader (CPL): _____ **Tel:** _____
Study Manager (SM): _____ **Tel:** _____
Study Statistician (SS): _____ **Tel:** _____

CRO _____ **CRO Study Tracking Number:** _____

Project Manager: _____ **Tel:** _____
Clinical Study Manager: _____ **Tel:** _____
Key Site Personnel:
Pharmacist: _____ **Tel:** _____
Topography: _____ **Tel:** _____
WatchPC: _____ **Tel:** _____

Monitoring CRO _____
Program Manager: _____ **Tel:** _____

Projected Date	Task or Milestone *(initiated by PMUSA SM unless noted otherwise)*
	PMUSA Clinical Study Team[♦] designs study.
	PMUSA Study Manager presents proposed study design for review to CE. Operations constructs study timeline & inserts in overall project timeline.
	PMUSA SM or CPL presents proposed study for review to RDE [**RDE Staff** *(JL)* or **R&C** *(GP)*] and/or **DRB** *(JN)*: ☐ Purpose and Objectives (scientific AND business) ☐ Relevant background support data ☐ Design (endpoints, time-event schedule, data analysis) ☐ Study timeline; how fits into overall project timeline ☐ Limitations (of design, schedule, results)
(days to IRB review)	
(~10 calendar days)	Protocol outline to CRO Protocol Writer Initiate contract process. Notify Legal of anticipated review date. Notify appropriate key partners: ☐ conventional cigarette(s) needed [qty (MC), smoke chem (PTL)] ☐ investigational cigarette(s) needed [qty, smoke chem (PTL)] ☐ Product Leader re Investigator's Brochure ☐ topography ☐ WatchPC ☐ monitoring CRO re monitoring plan ☐ bioanalytical assays ☐ ETS ☐ Discuss recruitment plan w/ CRO (Project Manager, Clin Study Manager, and Recruitment Manager)
	Draft protocol, attachments, ICF to PMUSA Study Manager, then PMUSA

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Source: https://www.industrydocuments.ucsf.edu/docs/hjpx0001

(~9 calendar days)	Clinical Study Team, for review. PMUSA Study Manager collates comments.
(~3 calendar days)	CRO Protocol Writer incorporates PMUSA comments.
(~10 calendar days)	Draft final protocol, attachments, ICF to PM Dir Clin Ops, then PM Legal, for review. PMUSA Study Manager collates final comments.
(~2 calendar days)	CRO Protocol Writer incorporates final PMUSA comments.
(~2 calendar days)	Final protocol, attachments, ICF to IRB Secretary and PMUSA Study Manager
(~7 calendar days)	**IRB review**

(in calendar weeks hereafter)

Subject recruitment begins once protocol IRB-approved.
PMUSA Study Manager notifies PMUSA Consumer Response Center.

Site initiation visit (required for any sites **NEW** to PMUSA)

PMUSA Study Manager reviews CRF.
Study initiation visit

Clinical conduct: **First subject, first visit (FSFV)**
Clinical conduct: **Last subject, last visit (LSLV)**

Clinical Database Lock (CDBL)
Routine monitoring begins(clinical conduct monitoring may occur earlier).

Listing by subject only of preliminary* 24-h urine creatinine concentration, volume, and Ae with bioplausibility evaluation results to Study Manager and Study Statistician.

In SHORT-TERM studies, preliminary subject listings by "treatment" group for COHb and smoking topography parameters MAY be requested by PMUSA Study Manager.*

Analytical Database Lock (ADBL)
Listings by subject only of selected preliminary* biomarker results as each locks to Study Manager and Study Statistician.

N.B.: Progressive, staged *ADBL may occur, with routine biomarkers locked at approx. 3 months after LSLV and any problematic biomarkers locked by 5 months after LSLV.*

Statistical Database Lock (SDBL) IF:

- SAP accepted.
- Monitoring completed.

N.B.: Progressive, staged *SDBL may occur, if progressive, staged ADBL occurred.*

All Tables and Figures for locked biomarkers provided to:

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Source: https://www.industrydocuments.ucsf.edu/docs/hjpx0001

- PMUSA Study Manager and Study Statistician for internal CE review.
- CRO Scientific Writer to begin Working Draft CSR.

Working Draft CSR to PMUSA Study Manager.

PMUSA Study Manager, reviews, collaborates with, and sends PMUSA comments to CRO Scientific Writer.

CRO Scientific Writer revises Working Draft CSR and sends Complete Draft CSR to PMUSA Study Manager.

PMUSA Clinical Study Team reviews Complete Draft CSR.
PMUSA Study Manager sends PMUSA comments to CRO Scientific Writer.

CRO Scientific Writer revises Complete Draft CSR and sends Final CSR to PMUSA Study Manager.

PMUSA Clinical Study Team reviews and accepts Final CSR.

LEGEND

° *PMUSA Clinical Study Team = PMUSA Clinical Program Leader (CPL) + PMUSA Study Mgr (SM) + PMUSA Study Statistician (SS) with input from Marketing, Bioanalytics (BA), Smoking Behavior (SB), and Dir. Clin Ops & Ops*

ADBL	*analytical database lock*
CE	*Clinical Evaluation*
CECP	*Clinical Evaluation Clinical Procedure*
CDBL	*clinical database lock*
COHb	*carboxyhemoglobin*
CRA	*Clinical Research Associate*
CRF	*case report form*
CRO	*Clinical Research Organization*
CSR	*clinical study report*
DRB	*Design Review Board*
ETS	*environmental tobacco smoke*
ICF	*informed consent form*
IRB	*Investigational Review Board*
MC	*Manufacturing Center*
PMUSA	*Philip Morris USA, Inc.*
PTL	*Product Testing Lab*
QC	*quality control*
R&C	*Research Results and Concepts meeting*
RDE	*Research, Development & Engineering*
SAP	*statistical analysis plan*
SDBL	*statistical database lock*

* preliminary data = non QCd data released before statistical database lock

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On occasion, PMUSA may request release of preliminary data for a specific biomarker in the form of data listings by analytical batch and summary statistics by" treatment" group to evaluate key clinical procedural compliance or to help make critical business or product development decisions.

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